

It has now been demonstrated, in a publication of which the present inventor, Anthony Adamis, is a coauthor, that in fact nucleic acids delivered to the inside of the human eye are therapeutically effective. This paper is attached hereto and marked as Exhibit A.

This paper describes Phase 1A and Phase 1B clinical trials using an anti-VEGF (Vascular Endothelial Growth Factor) nucleic acid molecule. The clinical trial was sponsored in part by the Harvard University-affiliated Massachusetts Eye and Ear Infirmary on patients afflicted with subfoveal choroidal neovascularization (CNV) secondary to age-related macular degeneration (AMD), a leading cause of blindness in the elderly.

This trial was conducted over the course of three months at 11 sites across the United States on qualified patients with subfoveal CNV secondary to AMD and whose visual acuity was between 20/100 and 20/400. The nucleic acid molecule, referred to as EYE001, was administered by intravitreal injection.

The studies strongly suggested that the nucleic acid molecule was more effective than another therapeutic regimen, one involving PDT (photodynamic therapy). A multi-centre, worldwide Phase 2/3 study is currently underway.

Thus, it has been conclusively demonstrated that nucleic acid molecules, when delivered to the interior of the human eye, have therapeutic benefit. Therefore, whether or not, as a general matter, the Examiner is correct that gene therapy was unpredictable and not routine at the time of the invention, in this particular case that issue is irrelevant, because the present inventor accurately predicted that nucleic acids, when delivered to the interior of the eye, would have therapeutic benefit. Thus, the failures of other workers in the field of gene therapy alluded to in the publications cited by the Examiner

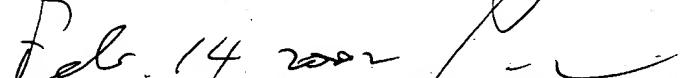
could not form the basis of a prediction that nucleic acid molecules would fail to show the therapeutic benefit in the eye; these molecules, in fact, do show such benefit. Further, nucleic acid molecules that bind to VEGF do not need to enter cells to inhibit angiogenesis, because VEGF is a secreted protein to which the nucleic acid molecule binds outside of cells. Thus, like the antibodies discussed in the present specification, the nucleic acid molecules essentially act like any other conventional drug, and issues such as numbers of cells that are transfected do not arise, since no transfection occurs.

In view of the above, it respectfully submitted that the application is in condition for allowance, and such action is requested.

If there are any charges, or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: Feb. 14, 2002

  
Paul T. Clark  
Reg. No. 30,162

Clark & Elbing LLP  
176 Federal Street  
Boston, MA 02110  
Telephone: 617-428-0200  
Facsimile: 617-428-7045  
F:\50069\50069.002002 Reply to OA.wpd



21559  
PATENT TRADEMARK OFFICE